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08/642,084

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/692,084	08/08/96	RODRIGUEZ	M 1199-1-001-C

HM21/0608

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EXAMINER	
DUFFY, P	
ART UNIT	**PAPER NUMBER**
1645	12

DATE MAILED: 06/08/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-19, is/are pending in the application.

Of the above, claim(s) 5-8, 15-18 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-4, 9-14 and 19 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims 1-19 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --

Response to Amendment

1. The Group and/or Art Unit of U.S. Patent application S.N. 08/697,084 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Technology Center 1600, Group 1640, Art Unit 1645.

2. The amendment filed 3-6-98 has been entered into the record. Claims 1-4, 9-14 and 19 are pending and under examination.

3. The text of Title 35 of the US Code not reiterated herein can be found in the previous office actions.

Rejections Maintained

Double Patenting

4. The rejection of claim 19 is rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of prior U.S. Patent No. 5,591,629 this is a double patenting rejection is maintained inasmuch as applicant has acknowledged this rejection (see top of page 3 of response) but has failed to traverse the rejection.

Claim Rejections - 35 USC § 102 or 103

Priority Date Assigned Claimed Invention

5. Applicants state that the instant claims are indeed entitled to the priority date of the application and provide a passage from the patent. This is not persuasive because the issued patent provides no written description support for antibodies O1, O4, A2B5, HNK-1, antigen

binding fragments thereof, or isolated or synthetic autoantibodies. Thus, one can not enable that which one has no written description support for. The claims are thus properly assigned the instant filing date as the priority date for art purposes. Applicants are directed *to Studiengesellschaft Khole m.b.H. v. Shell Oil Co.* 42 USPQ2d 1674 CAFC, 1997 which states:

> "In order for patent application to receive benefit of earlier filing date from prior application pursuant to 35 USC 120, earlier-filed applicant must contain disclosure which complies with first paragraph of 35 USC 112 for each claim in newly filed application, claim therefore complies with section 120 and acquires earlier filing date only if it could have been added to earlier application without introducing new matter."

6. The rejection of claims 1-4, 9 and 11-14 under 35 U.S.C. 102(b) as being anticipated by Miller et al (J. Neurosci., 14:6230-6238, 1994) is maintained for reasons made of record in Paper No. 9, mailed 10-2-97.

Applicants' assert that they are entitled to the priority date of the parent application and as such Miller et al is not available as prior art. This is not persuasive for the reasons set forth directly above.

New Rejections

Claim Rejections - 35 USC § 112

7. The rejection of claims 1-4, 9-14 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of stimulating remyelination or treating a demyelinating disease in a mammal by administering to a mammal an effective amount of the monoclonal antibody A2B5, it does not reasonably provide enablement for, isolated or synthetic autoantibodies or treatment of a demyelinating disease in mice or

humans. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims is maintained for reasons made of record in Paper No. 9, mailed 10-2-97.

Applicants' arguments have been carefully considered but are not persuasive for the reasons set forth below. Applicants assert that SCH94.03 and SCH79.08 have been deposited under the terms of the Budapest Treaty and thus all the requirements for deposit have been met, and submits the ATCC facsimile receipts to support deposit under the Budapest Treaty. As previously set forth this showing is insufficient because as set forth in the previous office action:

> "If the deposit has been made under the provisions of the Budapest Treaty, *filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of deposit and the complete name and full street address of the depository is required.*"

Applicants also assert that hybridomas O1 and O4 were a gift of Dr. S.E. Pfeiffer (University of Connecticut, Farmington CT) are known and publicly available on request from Dr. S. E. Pfeiffer. This is not persuasive because there is no evidence to support applicants allegation that these antibodies are publically available to any requestor and free from restrictions from Dr. S. E.

Pfeiffer. No declaration attesting to the allegation is provided. Applicants also assert that A2B5, HNK-1 and XXMEN-OE5 are readily available from the ATCC and provide attached pages of the ATCC Catalogue of Cell lines and Hybridomas. While this is persuasive for monoclonal antibody A2B5, it is not persuasive for HNK-1. XXMEN-OE5 is not specifically claimed. Specifically, the recitation of the catalogue states "This material is available under the conditions that you will not use it for commercial purposes or distribute it to third parties.". Thus, this hybridoma and monoclonal antibody is not freely commercially available to the public, it has access restrictions. Applicant is cautioned, that if free access and public availability is eventually demonstrated, then this reference not submitted will be cited as prior art against claim 19.

Applicants' assert *In re Fisher* 427 F.2nd 833, 839, 166 USPQ 18, 24 (CCPA 1970) in that as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement would be met. The evidence now submitted by applicants as Appendix C enables the scope of the claims 1-4, 9-14 19 for antibodies SCH 94.03, SCH 97.08, O1, O4, A2B2, HNK-1, antigen binding fragments thereof, ***provided that the deposit issues are appropriately settled, it does not provide support for isolate or synthetic autoantibodies having the characteristics thereof for the reasons set forth below.*** The evidence does not support isolated polyclonal antibodies such as autoantibodies or synthetic autoantibodies. Provided that deposit requirements are met, claims drawn to the scope set forth directly above would be allowable, in view that promotion of central nervous system remyelination stabilizes disease as set forth in the specification (pages 20-21) and the other antibodies which have been demonstrated to promote central nervous system remyelination would be expected to be similarly effective and that the demonstration of therapeutic effectiveness was demonstrated in the

Theiler's Virus-Induce Demyelinating Disease model and not the EAE mouse which has been demonstrated to lack predictable correlation with effective treatment in human disease.

As to isolated or synthetic autoantibodies, the specification fails to teach how to make isolated or synthetic autoantibodies with the characteristics of the monoclonal antibodies of the claims. The specification fails to teach from which animal these autoantibodies can be isolated. Autoantibodies are generally polyclonal and not monoclonal in nature. The population of autoantibodies from one outbred animal to another differs because the antibody genetic repertoire differs. Thus, the specification fails to teach how to predictably and reproducibly make a polyclonal antibody with the characteristics of the monoclonal antibody. Moreover, the art teaches that making polyclonal antibodies is unpredictable. The art specifically teaches that the production of polyclonal antiserum is variable and not readily reproducible. Autoantibodies are innately a polyclonal antibody population Campbell et al (page 3, column 2) teach that:

> "Polyclonal antiserum consists of a wide variety of antibody molecules of different specificity and affinity (Fig. 1.1). Each time an animal is bled, it yields a different 'cocktail' of such antibodies as its immune response to the injected and environmental antigen alters and B cell clones emerge and recede. The same animal can yield a highly specific antiserum directed against the chosen antigen in one bleed and a poor antiserum in another . The animal also has a limited lifespan and prior to the days of Mab technology, the death of a single rabbit could cause major problems is a diagnostic laboratory.
>
> There is an additional inter-animal variability among animals which cannot readily be inbred in the same way as small rodents can be inbred to yield pure strains with matching histocompatibility antigens (Section 3.4). While large 'outbred' animals such a s rabbits, sheep and goats, can yield a large quantity of specific antibody, their response to antigen is variable and it was often necessary to immunise up to 30 animals to obtain a high-affinity antiserum."

It would therefore require undue experimentation on the part of the skilled artisan to make autoantibodies with the same characteristics of a monoclonal antibody, absent undue experimentation.

8. Claims 1-4, 9-14 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to claim 1, 9 and 19, the claims are unclear in the recitation of "isolated or synthetic autoantibodies having the characteristics thereof" because it is unclear as to what characteristics are required (i.e. isotype, idiotype, IgG, IgM) by the autoantibody.

Status of Claims

9. All claims stand rejected.

Conclusion

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 6:30 AM to 3:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached at (703) 308-4310.

Patricia A. Duffy, Ph.D.
June 7, 1998

Patricia A. Duffy

Patricia A. Duffy, Ph.D.
Primary Examiner
Group 1640